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Prognostic value of REDS, SOFA, and D-dimer in critically ill COVID-19 patients with sepsis

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Introduction/Objective Early identification of high-risk patients with COVID-19-associated sepsis is essential for timely intervention and optimal ICU resource allocation. This study aimed to evaluate and compare the prognostic performance of risk-stratification of emergency department sepsis (REDS) and sequential organ failure assessment (SOFA) scores, alongside D-dimer levels, in predicting 28-day mortality among critically ill patients.

Methods A retrospective analysis was conducted on 163 critically ill adult patients with confirmed COVID-19 and sepsis (Sepsis-3 criteria) admitted to the intensive care unit of a tertiary center between November 2020 and May 2022. REDS, SOFA, and D-dimer values were assessed within 24 hours of ICU admission. Predictive value was evaluated using ROC analysis, logistic regression, and χ^2 automatic interaction detector (CHAID) decision tree modeling.

Results The overall 28-day mortality rate was 65.6%. REDS (AUC = 0.690) and SOFA (AUC = 0.680) demonstrated moderate predictive ability, while D-dimer showed lower accuracy (AUC = 0.632). REDS > 2 had the highest sensitivity (80.2%), and SOFA > 4 had the highest specificity (56.1%). Both REDS and SOFA were identified as independent mortality predictors. CHAID analysis recognized REDS as the strongest discriminator, stratifying mortality risk into three distinct groups (42.9%, 66.1%, and 84.5%).

Conclusion REDS and SOFA scores provide meaningful prognostic value in patients with COVID-19-related sepsis. REDS demonstrated a slight advantage and may serve as a simple and effective bedside tool for early risk stratification in clinical practice and future viral pandemics.

Keywords: COVID-19; sepsis; REDS score; SOFA score; prognosis; mortality

INTRODUCTION

Critically ill patients with COVID-19 and sepsis remain among the most vulnerable in intensive care units (ICUs), with persistently high mortality rates despite advances in supportive care [1, 2, 3]. The convergence of viral pneumonia, immune dysregulation, and sepsis-induced multiorgan failure creates complex clinical scenarios, underscoring the urgent need for reliable early prognostic tools [4]. Timely risk stratification is essential to inform therapeutic decisions, optimize resource allocation, and improve patient outcomes. While numerous studies have explored individual biomarkers and severity scores, there is still no consensus on the most effective approach for early mortality prediction in this high-risk group [5, 6, 7]. Notably, risk-stratification of emergency department sepsis (REDS) scoring system has been shown to be a simple and objective tool for risk stratification in patients with suspected sepsis, although these studies did not include patients with COVID-19 [8].

This study provides novel insights by directly comparing the prognostic performance of three early indicators – the sequential organ failure assessment (SOFA) score, REDS score, and D-dimer levels – within the first 24 hours

of ICU admission in COVID-19 patients with sepsis. Unlike prior research that typically assessed single markers or lacked rigorous validation, our study integrates multiple established tools and employs advanced statistical techniques, including bootstrap-adjusted multivariate logistic regression and χ^2 automatic interaction detector (CHAID) decision tree modeling, to enhance predictive power and internal validity [9, 10, 11].

The most notable finding is the potentially valuable prognostic role of the REDS score in predicting 28-day mortality, supported by receiver operating characteristic (ROC) analysis, multivariate models, and decision tree classification. A simplified model based on REDS thresholds effectively stratified patients into clinically relevant risk groups, supporting its utility in ICU triage and early management. The use of bootstrap validation further mitigates limitations common to retrospective studies, such as small sample size and data skewness, enhancing the robustness of our conclusions.

This study was conducted in critically ill COVID-19 patients with sepsis. While the findings provide valuable insights for this specific population, their applicability to future pandemics caused by similar viral pathogens remains to be investigated. Given the challenges

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posed by comorbidities, immunosuppression, and variable vaccine responsiveness, our results underscore the potential importance of accurate, evidence-based prognostic tools in guiding clinical decisions. The objective of this study was to assess and compare the prognostic accuracy of the SOFA score, REDS score, and D-dimer levels in predicting 28-day mortality, using comprehensive and statistically rigorous methodologies. These findings contribute to the expanding literature on multidimensional and machine learning-assisted approaches in critical care and support further external validation in larger, diverse cohorts.

METHODS

This retrospective observational study was conducted at the Institute for Pulmonary Diseases of Vojvodina, within the Clinic for Intensive Care Medicine and Pulmonary Vascular Diseases, Department for Intensive Care and Intoxications Level 3. The study population included 163 critically ill patients with confirmed COVID-19 and sepsis who were admitted to the ICU between November 2020 and May 2022.

Eligibility criteria included adult patients (≥ 18 years) with COVID-19 confirmed via reverse transcription-polymerase chain reaction or rapid antigen testing using nasopharyngeal swabs. All patients met Sepsis-3 criteria, requiring documented or suspected infection and an acute increase of ≥ 2 points in the SOFA score [12]. To minimize confounding, we excluded individuals with advanced immunocompromised states (e.g., HIV/AIDS, transplant recipients, active cancer, autoimmune diseases), as well as pregnant or breastfeeding women.

Demographic, clinical, and laboratory data were collected from medical records within the first 24 hours of ICU admission. Variables necessary for calculating the SOFA and REDS scores were extracted from documentation and verified by two independent reviewers. Laboratory tests, including D-dimer levels, were performed using the VIDAS® D-Dimer Exclusion II assay (BioMérieux, Marcy-l'Étoile, France), which is based on an enzyme-linked fluorescent assay technique and analyzed on the VIDAS 3 platform.

The primary outcome was 28-day all-cause mortality. Statistical analyses were performed using SPSS Version 26.0 (IBM Corp., Armonk, NY, USA), MedCalc Statistical Software v20.2 (MedCalc Software Ltd., Ostend, Belgium). A two-tailed p -value < 0.05 was considered statistically significant.

Statistical analysis

Continuous variables were summarized as medians with interquartile ranges, while categorical variables were presented as frequencies and percentages. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Between-group comparisons were conducted using the Mann-Whitney U test for non-normally distributed data and the χ^2 or Fisher's exact test for categorical

variables, depending on expected cell frequencies. To evaluate the discriminatory power of the SOFA score, REDS score, and D-dimer levels for predicting 28-day mortality, ROC curve analyses were performed. The Youden index was applied to determine optimal cut-off values for each marker. Diagnostic performance was assessed through sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), each with corresponding 95% confidence intervals. Multivariate logistic regression analysis was conducted to identify independent predictors of 28-day mortality, with internal validation performed through bootstrapping (1000 iterations) to improve model robustness and minimize overfitting. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test by comparing observed and expected mortality across deciles of predicted risk. Additionally, a CHAID decision tree analysis was employed to explore variable interactions and stratify mortality risk groups based on REDS, SOFA, and D-dimer, allowing identification of key thresholds and clinically relevant decision nodes.

Ethics: The study protocol received ethical approval from the Ethics Committee of the Institute for Pulmonary Diseases of Vojvodina (No. 9-II/3, February 24, 2022) and the Faculty of Medicine, University of Novi Sad (No. 01-39/190/1, May 13, 2022).

RESULTS

In this study involving 163 critically ill COVID-19 patients with sepsis, the prognostic performance of three early clinical indicators – SOFA score, REDS score, and D-dimer levels – was evaluated within the first 24 hours of ICU admission for their ability to predict 28-day mortality. In this cohort, the prevalence of comorbidities varied, with hypertension (55.8%) and diabetes mellitus (27%) being the most common (Figure 1). Although patients with malignancy exhibited the highest mortality rate (90.9%), this did not reach statistical significance ($p = 0.062$), likely due

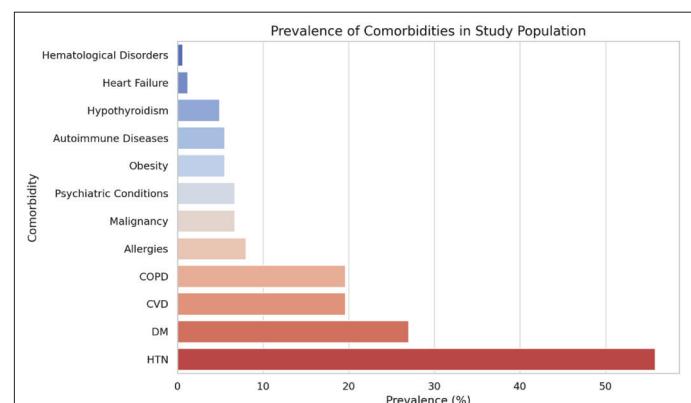


Figure 1. Prevalence of comorbidities in the patient cohort, with hypertension (HTN) (55.8%) and diabetes mellitus (DM) (27%) as the most frequent conditions; cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD) rank third and fourth in prevalence, respectively; this distribution highlights the common occurrence of multiple underlying diseases that may influence patient prognosis and clinical management

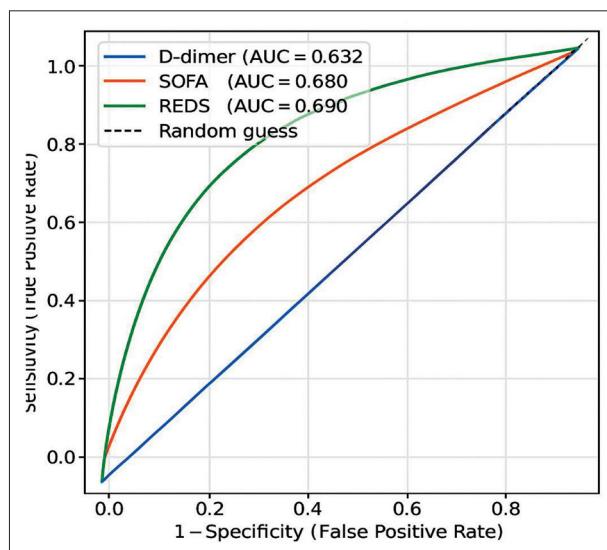


Figure 2. ROC curves for D-dimer, sequential organ failure assessment (SOFA), and risk-stratification of emergency department sepsis (REDS) scores showing their predictive accuracy for 28-day mortality; AUC values indicate the discriminative performance of each tool

to the small subgroup size. Other comorbidities such as chronic obstructive pulmonary disease, cardiovascular disease, and diabetes showed elevated mortality proportions but without statistically significant differences between survivors and deceased. The absence of significant associations may reflect limited statistical power or heterogeneous effects of individual comorbidities on 28-day outcomes. Overall, these findings suggest that while comorbid conditions are prevalent in critically ill patients, their isolated impact on short-term mortality requires further investigation in larger cohorts to clarify their prognostic value.

ROC curve analysis demonstrated moderate discriminative ability across all three parameters (Figure 2). The REDS score yielded the highest Youden index (0.293; 95% CI: 0.148–0.403), followed by the SOFA score (0.288; 95%

CI: 0.162–0.420) and D-dimer (0.255; 95% CI: 0.132–0.377). The optimal cut-off values identified were REDS > 2, SOFA > 4, and D-dimer > 1425 µg/L. Notably, the confidence interval for D-dimer's cut-off value was wide (1028–8253 µg/L), indicating potential variability in its discriminatory capacity.

D-dimer (AUC = 0.632) shows modest predictive value, slightly better than chance. SOFA (AUC = 0.680) performs better with moderate accuracy. REDS (AUC = 0.690) is the best among the three, though only marginally superior to SOFA (Table 1). All models have AUCs between 0.6 and 0.7, indicating weak to moderate predictive power. Based on the ROC analysis for this sample, although none of the scores are strong predictors on their own, both REDS and SOFA demonstrated statistically significant differences between survivors and non-survivors ($p < 0.001$), highlighting their value as useful prognostic tools within a comprehensive clinical assessment.

Table 1. AUC ROC curve analysis for D-dimer, sequential organ failure assessment (SOFA) and risk-stratification of emergency department sepsis (REDS) scores for predicting 28-day mortality

| Parameters | AUC ROC | SE | 95% CI for AUC ROC | p |
|------------|---------|-------|--------------------|-------------------|
| D-dimer | 0.632 | 0.047 | 0.551–0.707 | 0.005 |
| SOFA | 0.680 | 0.042 | 0.603–0.751 | < 0.001 |
| REDS | 0.690 | 0.043 | 0.613–0.760 | < 0.001 |

SE – standard error; CI – confidence interval; p – probability that AUC differs from 0.5 (no discrimination); all AUC values 0.6–0.7 indicate moderate discrimination; p-values indicate significance of AUC versus 0.5 (no discrimination)

In terms of diagnostic accuracy, REDS > 2 demonstrated the highest sensitivity (80.2%) and NPV (71.3%), while SOFA > 4 achieved the highest specificity (56.1%) and PPV (75.5%). D-dimer > 1425 µg/L showed a sensitivity of 76.5%, specificity of 49.1%, PPV of 73.6%, and NPV of 52.9% (Table 2). Despite the observed differences in point estimates, the overlapping confidence intervals for

Table 2. Optimal cut-off, sensitivity, specificity, PPV and NPV for D-dimer, SOFA and REDS

| Variable | Youden index | 95% CI Youden index | Optimal cut-off value | 95% CI for cut-off value | SENS (%) | SPEC (%) | PPV | NPV |
|----------|--------------|---------------------|-----------------------|--------------------------|----------|----------|------|------|
| D-dimer | 0.25 | 0.13–0.37 | > 1425 | > 1028 – > 8253 | 76.47 | 49.09 | 73.6 | 52.9 |
| SOFA | 0.28 | 0.16–0.42 | > 4 | > 3 – < 6 | 72.64 | 56.14 | 75.5 | 52.5 |
| REDS | 0.29 | 0.14–0.40 | > 2 | > 1 – < 4 | 80.19 | 49.12 | 61.2 | 71.3 |

CI – confidence interval; SENS – sensitivity; SPEC – specificity; PPV – positive predictive value; NPV – negative predictive value; SOFA – sequential organ failure assessment; REDS – risk-stratification of emergency department sepsis

Table 3. Individual REDS parameters: comparison between survivors and non-survivors (n = 163)

| REDS Component | Survivors n = 56 | Non-survivors n = 107 | χ^2 (df) | p |
|---|------------------------------------|--------------------------------------|---------------|--------------|
| Age ≥ 65 years | 24 (42.9%) | 61 (57.0%) | 2.95 (1) | 0.086 |
| GCS < 15 | 16 (28.6%) | 55 (51.4%) | 7.79 (1) | 0.005 |
| SBP < 100 mmHg | 13 (23.2%) | 28 (26.2%) | 0.17 (1) | 0.680 |
| RR ≥ 22/min | 30 (53.6%) | 70 (65.4%) | 2.18 (1) | 0.140 |
| Lactate (categorical: ≤ 2 / 2.1–3.9 / ≥ 4 mmol/L) | 36 (64.3%) / 15 (26.8%) / 5 (8.9%) | 42 (39.3%) / 46 (43.0%) / 19 (17.8%) | 9.34 (2) | 0.009 |
| Albumin < 27 g/L | 19 (34.5%) | 41 (38.7%) | 0.27 (1) | 0.607 |
| INR ≥ 1.3 | 17 (30.9%) | 37 (34.9%) | 0.26 (1) | 0.610 |
| Refractory hypotension + lactate: – RH absent – RH + lactate < 2 – RH + lactate ≥ 2.1 | 48 (85.7%) 5 (8.9%) 3 (5.4%) | 72 (67.3%) 9 (8.4%) 26 (24.3%) | 9.12 (2) | 0.010 |

REDS – risk-stratification of emergency department sepsis; GCS – Glasgow coma scale; SBP – systolic blood pressure; RR – respiratory rate; INR – international normalized ratio; RH – refractory hypotension; lactate values are categorized as ≤ 2.0, 2.1–3.9, and ≥ 4.0 mmol/L; albumin < 27 g/L and INR ≥ 1.3 indicate hypoalbuminemia and coagulopathy, respectively; refractory hypotension in combination with elevated lactate (≥ 2.1 mmol/L) reflects the highest circulatory risk subgroup; χ^2 values with degrees of freedom (df) were used to assess the association between each REDS component and 28-day mortality

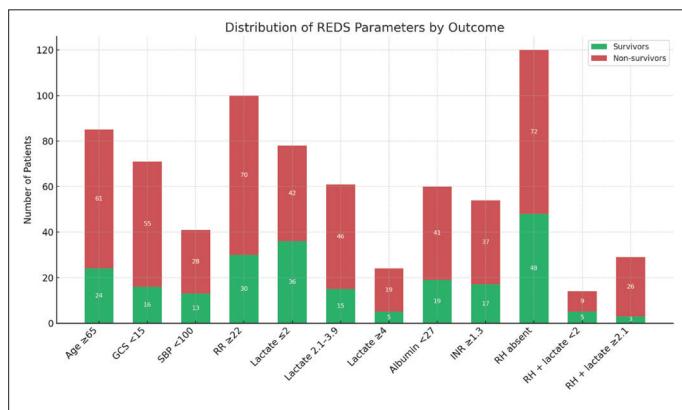


Figure 3. Distribution of risk-stratification of emergency department sepsis (REDS) parameters by outcome; lactate values are expressed in mmol/L, and albumin in g/L; GCS – Glasgow coma scale; SBP – systolic blood pressure; RR – respiratory rate; INR – international normalized ratio; RH – refractory hypotension

the Youden index suggest that none of the three markers was statistically superior in isolation.

In our research, three REDS parameters showed statistically significant associations with mortality outcomes (Table 3). Patients with Glasgow coma scale < 15 had over 75% mortality, indicating a strong correlation between severe neurological impairment and death. Similarly, approximately 80% of patients with lactate levels ≥ 4 mmol/L did not survive, underscoring the prognostic importance of elevated lactate. Furthermore, more than 85% of patients exhibiting refractory hypotension combined with lactate ≥ 2.1 mmol/L died, highlighting this combination as a potent clinical marker of high mortality risk. Among the eight REDS components, these variables demonstrated the most pronounced and significant differences between survivors and non-survivors, while other parameters such as systolic

blood pressure < 100 mmHg and albumin < 27 g/L showed no significant discrimination (Figure 3). Despite variability in individual component performance, the composite REDS score exhibited superior discriminatory ability (AUROC = 0.69, $p < 0.001$) by integrating all variables, supporting its role as a comprehensive bedside risk stratification tool. These findings suggest that while certain REDS components have stronger individual prognostic value, the aggregate score remains the preferred measure for clinical application and may benefit from further optimization in future studies.

In the multivariate logistic regression model, both the REDS and SOFA scores were identified as independent predictors of mortality (Table 4). Each one-point increase in the REDS and SOFA scores was associated with a 22% increase in the odds of death (OR = 1.22, $p \leq 0.05$ for both). Male sex was also independently associated with increased mortality risk (OR = 2.78, $p = 0.029$). Other variables, including hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and allergies, were not statistically significant predictors in the adjusted model. Logistic regression analysis and combined ROC curves further supported the enhanced prognostic utility when these variables were used in tandem.

To assess the predictive value of clinical variables for mortality in critically ill COVID-19 patients with sepsis, a logistic regression analysis was performed using the bootstrap method with 1000 samples (Table 5). This approach allowed for a more robust estimation of the model parameters, reducing potential bias and improving the reliability of confidence intervals in small and potentially non-normally distributed datasets.

Table 4. Logistic regression summary table – multivariate model

| Variable | B (Beta) | p | Exp(B) (OR) | Interpretation |
|------------|----------|-------|-------------|--|
| SOFA score | 0.204 | 0.024 | 1.226 | Each one-point increase in SOFA raises death risk by 22.6% |
| D-dimer | 0.000 | 0.050 | 1.000 | Marginally significant; very weak or negligible effect |
| REDS score | 0.203 | 0.050 | 1.225 | Each one-point increase in REDS raises death risk by 22.5% |
| Sex (Male) | 1.018 | 0.012 | 2.766 | Males have 2.77 times higher risk of death compared to females |
| HTN | 0.391 | 0.332 | 1.479 | Not significant when adjusted for other variables |
| DM | 0.147 | 0.755 | 1.159 | Not significant |
| CVD | 0.073 | 0.883 | 1.075 | Not significant |
| COPD | 0.724 | 0.145 | 2.062 | Not statistically significant |
| Allergies | 1.042 | 0.162 | 2.834 | Not statistically significant |

Logistic regression analysis of predictors of mortality in critically ill COVID-19 patients; B – regression coefficient; Exp(B) – odds ratio (OR); p-values ≤ 0.05 are considered statistically significant; in the multivariate logistic regression model, each 1-point increase in sequential organ failure assessment (SOFA) or risk-stratification of emergency department sepsis (REDS) scores was associated with an approximately 22% increase in the odds of 28-day mortality (OR = 1.22 for SOFA and OR = 1.225 for REDS; $p \leq 0.05$ for both); male sex was also identified as an independent predictor of mortality, with males having nearly 2.8 times higher risk compared to females; other comorbidities [hypertension (HTN), diabetes mellitus (DM), cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), allergies] did not show statistically significant associations with mortality in the multivariate model

Table 5. Multivariate logistic regression with bootstrap (1000 samples)

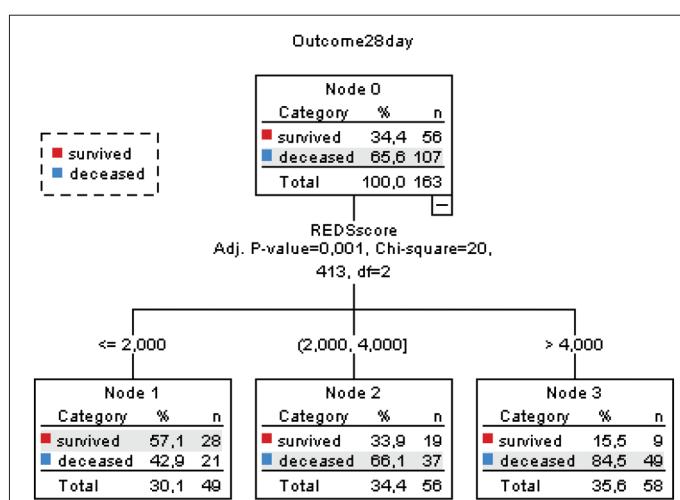
| Variable | B (Coefficient) | Std. Error | p (Sig. 2-tailed) | 95% CI – Lower | 95% CI – Upper |
|------------|-----------------|------------|-------------------|----------------|----------------|
| SOFA score | 0.188 | 0.077 | 0.005 | 0.044 | 0.355 |
| D-dimer | 0.000 | 0.000 | 0.143 | 0.000 | 0.000 |
| REDS score | 0.195 | 0.107 | 0.049 | 0.014 | 0.448 |
| Constant | -1.421 | 0.525 | 0.003 | -2.527 | -0.447 |

(Outcome: in-hospital mortality) – multivariate logistic regression with bootstrap resampling (1000 samples) identified sequential organ failure assessment (SOFA) and risk-stratification of emergency department sepsis (REDS) scores as independent predictors of mortality in critically ill COVID-19 patients with sepsis; the 95% confidence intervals for SOFA and REDS excluded zero, supporting their prognostic relevance

Table 6. Observed vs. expected 28-day mortality by deciles of predicted risk

| Decile of Predicted Probability | Observed Deaths (n) | Total Patients (n) | Observed Mortality (%) | Expected Deaths (n) | Expected Mortality (%) |
|---------------------------------|---------------------|--------------------|------------------------|---------------------|------------------------|
| 1 (lowest risk) | 5 | 16 | 31.3 | 10.5 | 65.6 |
| 2 | 5 | 16 | 31.3 | 10.5 | 65.6 |
| 3 | 10 | 17 | 58.8 | 11.2 | 65.9 |
| 4 | 10 | 16 | 62.5 | 10.5 | 65.6 |
| 5 | 9 | 16 | 56.3 | 10.5 | 65.6 |
| 6 | 15 | 17 | 88.2 | 11.2 | 65.9 |
| 7 | 11 | 16 | 68.8 | 10.5 | 65.6 |
| 8 | 15 | 17 | 88.2 | 11.2 | 65.9 |
| 9 | 14 | 16 | 87.5 | 10.5 | 65.6 |
| 10 (highest risk) | 13 | 16 | 81.3 | 10.5 | 65.6 |
| Total | 107 | 163 | 65.6 | 107 | 65.6 |

The table displays the observed and expected mortality within each decile of predicted death probability; the "observed mortality (%)" column shows the actual mortality rate in each decile, while the "expected mortality (%)" reflects the model's predicted mortality; consistency between observed and expected mortality across deciles indicates good calibration of the predictive model

**Figure 4.** Decision tree model stratifying 28-day mortality outcomes using risk-stratification of emergency department sepsis (REDS) score

The use of bootstrap logistic regression represents a novel methodological aspect of this study, ensuring more stable estimates of the regression coefficients and confidence intervals compared to traditional methods. This technique enhances statistical robustness, particularly in clinical datasets with skewed distributions and heterogeneous patient populations. Our findings confirm the independent prognostic significance of both the SOFA and REDS scores, while D-dimer did not reach statistical significance in the multivariate model.

The calibration of the predictive model was evaluated across deciles of predicted mortality risk using the Hosmer-Lemeshow goodness-of-fit test, which yielded $p > 0.05$ for the overall model ($\chi^2 = 11.285$; $df = 8$; $p = 0.186$). This indicates that there was no statistically significant difference between the observed and expected mortality rates across all risk deciles (Table 6). The observed and expected mortality frequencies, as presented in Table 6, demonstrate satisfactory model calibration and internal validity, supporting its ability to stratify patients reliably across the full spectrum of disease severity. Such adequate calibration strengthens the model's clinical applicability by ensuring

stable and trustworthy risk estimates that can aid early decision-making, optimize resource allocation, and guide individualized management strategies in critically ill patients.

The CHAID decision tree analysis was employed to identify the most relevant predictors of 28-day mortality in critically ill patients. Among the evaluated variables – SOFA score, REDS score, and D-dimer – only the REDS score remained in the final model, highlighting its important predictive value within this cohort (Figure 4). The resulting tree had a simple structure with one major split (depth = 1), dividing patients into three terminal nodes based on REDS score thresholds. Mortality rates increased progressively across these groups, from 42.9% in patients with REDS ≤ 2 , to 66.1% in those with scores between 2.1–4.0, and reaching 84.5% in those with scores > 4.0 . This stratification demonstrates the REDS score's strong discriminatory ability and practical clinical utility for early risk assessment. The simplicity of the model enhances its applicability in real-time decision-making; however, the absence of internal or external validation limits the ability to generalize these findings beyond the current sample and warrants further evaluation in broader patient populations.

DISCUSSION

This study provides important insights into the prognostic performance of early clinical indicators – SOFA score, REDS score, and D-dimer – in critically ill COVID-19 patients with sepsis. Consistent with prior research, our findings show that while none of these markers alone achieves ideal accuracy, the REDS score demonstrates the highest sensitivity and NPV, underscoring its value as an effective initial triage tool to identify low-risk patients. This aligns with the intended role of rapid assessment tools for early deterioration, highlighting their broader clinical applicability in patients with sepsis and the potential to improve timely interventions and resource allocation [7, 9, 11].

Conversely, the SOFA score exhibited superior specificity and PPV, reinforcing its utility in confirming patients at higher mortality risk. These complementary characteristics suggest that SOFA and REDS scores serve distinct but synergistic roles in risk stratification [12–15]. The D-dimer, despite moderate sensitivity, showed wide confidence intervals around cut-off points, reflecting biological variability and highlighting the challenges of relying on coagulation markers alone for prognostication in this context. This observation resonates with emerging literature documenting inconsistent predictive utility of D-dimer across heterogeneous COVID-19 cohorts [16–19].

Importantly, the overlapping confidence intervals for the Youden indices emphasize that these markers are best utilized in combination rather than isolation, supporting a multimodal prognostic strategy. Clinically, a REDS score > 2 may serve as an early alert prompting closer monitoring and resource allocation, whereas a SOFA score > 4 could guide escalation of care decisions. Incorporation of D-dimer into composite models may add incremental value but requires further validation [20, 21].

Our multivariate logistic regression analysis substantiates the independent prognostic significance of both REDS and SOFA scores, with each point increase correlating with a 22% rise in mortality odds, even after adjustment for key comorbidities. This reinforces the robustness of these scores as bedside tools reflecting organ dysfunction severity rather than mere comorbidity burden. Interestingly, common comorbidities including hypertension and diabetes were not independently predictive, suggesting their effects may be mediated through clinical deterioration captured by these scoring systems [22]. Male sex emerged as an additional independent risk factor, consistent with documented sex disparities in COVID-19 outcomes [23].

The CHAID decision tree analysis further illustrates the clinical utility of the REDS score by stratifying patients into clear mortality risk groups based on simple thresholds. In the era of precision medicine, such machine-learning-based models offer scalable, interpretable tools to augment clinician judgment and tailor management strategies [24]. Our findings support integrating decision tree models with validated scores like REDS to enhance real-time ICU triage, ultimately improving individualized care and resource optimization.

Calibration analysis is an important step in evaluating predictive models across diverse clinical populations [25, 26]. For example, it has been applied in neurological patients, and in our study, the model showed good alignment between observed and predicted 28-day mortality across risk deciles in critically ill COVID-19 patients with sepsis, supporting its potential reliability for early clinical decision-making.

During the COVID-19 pandemic, careful prioritization of emergency and elective cases became a critical aspect of hospital management, with clear guidelines emphasizing that only urgent, non-deferrable cases should be treated immediately to reduce hospital crowding and protect both patients and healthcare staff [27]. The identification of effective laboratory biomarkers that could stratify patients at risk of developing severe forms of the disease is imperative

to ensure they receive prompt medical treatment [28]. In this context, the implementation of relatively simple and rapidly applicable scoring systems such as REDS and SOFA can facilitate the early identification of high-risk patients, enabling clinicians to prioritize treatment and optimize outcomes. These tools, together with biomarker such as D-dimer may play an important role in guiding appropriate and timely therapy in patients with severe forms of COVID-19 and sepsis.

Limitations of this study include its retrospective design, single-center setting, and modest sample size, which may affect generalizability. The absence of external validation warrants cautious interpretation and underlines the need for prospective, multicenter studies to confirm and refine these predictive models.

CONCLUSION

This study demonstrates that among critically ill COVID-19 patients with sepsis, the REDS score is a robust and independent predictor of 28-day mortality, outperforming both SOFA score and D-dimer levels in risk stratification. The application of CHAID decision tree analysis further confirms the REDS score's practical utility in categorizing patients into distinct mortality risk groups, facilitating timely clinical decision-making. Bootstrap-validated logistic regression reinforces the reliability of these findings despite the retrospective design and sample size limitations. These results support the integration of the REDS score into ICU protocols to improve early identification of high-risk patients and optimize resource allocation.

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Прогностички значај *REDS*, *SOFA* и Д-димера код критично оболелих од ковида 19 са сепсом

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САЖЕТАК

Увод/Циљ Рано препознавање болесника са високим ризиком од смртног исхода код сепсе настале услед ковида 19 од суштинског је значаја за правовремену интервенцију и оптималну расподелу ресурса у јединици интензивног лечења. Циљ рада био је да се процени и упореди прогностичка вредност скорова *REDS* (Скор за стратификацију ризика сепсе на одељењу хитне помоћи) и *SOFA* (Скор процене секвенцијалног попуштања органа), заједно са нивоом Д-димера, у предикцији 28-дневног морталитета код тешко оболелих болесника.

Методе Ретроспективна анализа обухватила је 163 одрасла болесника са потврђеним ковидом 19 и сепсом (критеријуми Сепса-3), лечена у јединици интензивног лечења терцијарног центра у периоду од новембра 2020. до маја 2022. *REDS*, *SOFA* и вредности Д-димера процењене су у року од 24 сата од пријема. Прогностичка вредност анализирана је помоћу ROC анализе, логистичке регресије аутоматским

детектором интеракција (Хи-квадрат) (*CHAID*) моделовања стабла одлуке.

Резултати Укупна 28-дневна смртност износила је 65,6%. *REDS* ($AUC = 0,690$) и *SOFA* ($AUC = 0,680$) показали су умерену предиктивну способност, док је Д-димер имао нижу тачност ($AUC = 0,632$). $REDS > 2$ имао је највећу сензитивност (80,2%), док је *SOFA > 4* показао највећу специфичност (56,1%). *REDS* и *SOFA* идентификовани су као независни предиктори смртности. *CHAID* анализа издвојила је *REDS* као најјачи дискриминатор, који је стратификовао болеснике у три групе ризика са стопама смртности од 42,9%, 66,1% и 84,5%.

Закључак Скорови *REDS* и *SOFA* имају значајну прогностичку вредност код болесника са ковидом 19 повезаним сепсом. *REDS* је показао благу предност и може послужити као једноставан и ефикасан алат за рану стратификацију ризика у клиничкој пракси и будућим вирусним пандемијама.

Кључне речи: ковид 19; сепса; скор *REDS*; скор *SOFA*; прогноза; морталитет